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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,783	12/26/2000	David R. Goodlett	P-IS 4369	3333

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EXAMINER	
MAHATAN, CHANNING	
ART UNIT	PAPER NUMBER
1631	15

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/748,783	GOODLETT, DAVID R.	
	Examiner	Art Unit	
	Channing S. Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-16 and 18-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-16 and 18-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

APPLICANTS' ARGUMENTS

Applicants' arguments in Paper No. 14, filed 17 April 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-5, 7-16, and 18-70. Claims 6 and 17 have been cancelled as indicated in Paper No. 14, filed 17 April 2003.

Provisional Obviousness-Type Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 U.S.P.Q. 2d 2010 (Fed. Cir, 1993); *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982); *In re Vogel*, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970); and, *In re Thorington*, 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

Claims 37-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of co-pending Application No. 09/748,793. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims define an invention which is a method of identifying a polypeptide with such similarity making the inventions have overlapping embodiments. It is acknowledged that the claim sets are structurally different, however, all limitations are present among the claims as a whole and thus encompass overlapping embodiments.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims Rejected Under 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 12, 24, 25, 27, 33-36, 52-57, 59, 60, and 66-70 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Yates et al. (Mass Spectrometry and the Age of the Proteome, Journal of Mass Spectrometry. 1998, Volume 33, pages 1-19). This ground of rejection is newly introduced upon further consideration of the prior art as a whole and the applicants' arguments.

It should be noted applicants' specification states: "Simultaneous determination of the mass of a subset of polypeptides can be performed, for example, in the absence of selection of a single ion for mass determination. For example, several polypeptides can be selected rather than a single ion (Masselon et al., Anal. Chem. 72:1918-1924 (2000))." (page 55, lines 8-17). Further, the applicants' disclosure states: "...simultaneous determination of masses of a subset of polypeptides can be performed in the absence of single ion selection or in the absence of ion selection in a source region (see Figure 2). In such a case, the fragment ions obtained are deconvoluted to determine which ions are associated with a particular parent polypeptide and therefore useful as a characteristic associated with the parent polypeptide." (page 55, lines 18-28 of the Specification). Thus, in the "absence of ion selection" all ions are fragmented at the source and followed by the simultaneous mass spectrometer analysis, wherein all ions (fragments) are subjected to the mass spectrometer (Figure 2B). Claims 1, 2, 4, 5, 12, 41, and 44-51 broadly encompass the presence of ion selection.

Yates describes various ionization and mass analysis techniques for the identification of proteins in mixtures using a combination of enzymatic proteolysis, liquid chromatographic separation, mass spectrometry and computer algorithms which match peptide mass spectra to sequences in a database (Abstract). The method(s) includes 1) determination of two or more

characteristics (one of which being mass of the fragment) (page 7, column 2, lines 32-36; page 9, column 2, lines 10-62); 2) comparing the characteristics and identifying the polypeptide from an annotated polypeptide index (page 7, column 2, lines 58-65; page 9, column 1, lines 52-60). 3) determining one or more additional characteristics, wherein the characteristics include peptide mass, m/z value(s), translated sequence fidelity, reading frame, amino acid composition/sequence, polypeptide origin/organism , nucleotide sequence, or order of elution on a chromatographic medium (page 7, column 1, lines 27-31; page 7, column 2, line 43 to page 9, column 1, line 5; page 9, column 1, lines 25-28 and 43-45; Figures 3, 4, and 6; page 12, line 22 to page 13, column 2, line 8; thus meeting the limitation of 5 or more characteristics associated with said polypeptide); 4) comparing the characteristics to an annotated polypeptide index; and 5) repeating these steps. Yates describes the use of time-of-flight mass (TOF) spectrometers to identify proteins where all ions (i.e. peptide fragments) are simultaneously (fragments are separated based upon kinetic energy differences corresponding to varying fragment masses) subjected to the mass spectrometer in a field free region (i.e. absence of ion selection) and (page 5, column 1, line 4 to column 2, line 21). The author illustrates in Figure 7 the use of a TOF spectrometer to identify proteins where: 1) a parent polypeptide is selected (circled) from a population of polypeptides; 2) the parent polypeptide is subjected to proteolysis; 3) the fragments are collected and analyzed by time-of flight; and 4) the data obtained from the TOF is used to search sequence databases to identify the protein. Thus, Yates clearly anticipates the claimed invention.

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The above 35 U.S.C. § 102 (b) reference to applicants' specification regarding "simultaneous" and "absence of ion selection" is further applied to the below 35 U.S.C. § 103(a) rejection(s), wherein claims 1-5, 7-12 and 37-51 broadly encompass the presence of ion selection.

Claims 1-5, 12, 13-16, 23-27, 33-36, 48-60, and 66-70 are rejected under 35 U.S.C. § 103 as obvious over Yates (Mass Spectrometry and the Age of the Proteome, Journal of Mass Spectrometry. 1998, Volume 33, pages 1-19); taken in view of Gygi et al. (Quantitative analysis of complex protein mixtures using isotope-coded affinity tags, Nature Biotechnology, 17 October 1999, Volume 17, pages 994-999).

Yates et al. is deficient to provide for the elements of quantitation of the polypeptides identified. Gygi et al. describes an approach for the accurate quantification and concurrent sequence identification of individual proteins within complex mixtures in a single automated operation (Abstract; page 995, column 2, lines 1-2). The ICAT strategy (Figure 2 and page 995, column 1-2, lines 1-8 and 1-2, respectively) provides a broadly applicable solution to quantitative proteome analysis, particularly mass spectrometry (page 998, column 2, lines 43-65).

Thus, it would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the method of quantitating the proteins identified in a single automated operation, as taught by Gygi et al. with Yates a method of identifying polypeptide(s) by mass spectrometry utilizing databases. Gygi et al. provides for various motivations to utilize the described ICAT strategy as it is widely applicable to compare small changes of protein expression in cells and tissues accurately (Abstract; and page 997, column 1, lines 27-38) and the single automated operation would increase efficiency over separate operations by 1) reducing complexity of the peptide mixture; 2) allowing for chemical reactions in the presence of chemicals without reactive a thiol group; 3) eliminating contaminates; and 4) being compatible with any biochemical, immunological, or cell biological fraction method; 5) the redundancy in quantification and identification of multiple cysteines; and 6) being extendable to include reactivity toward other functional groups (page 998, column 1, line 20 to column 2, line 43).

Claims 1-5, 7-16, and 18-70 are rejected under 35 U.S.C. § 103 as being clearly anticipated by Yates (Mass Spectrometry and the Age of the Proteome, Journal of Mass Spectrometry. 1998, Volume 33, pages 1-19); taken in view of Gygi et al. (Quantitative analysis of complex protein mixtures using isotope-coded affinity tags, Nature Biotechnology, 17 October 1999, Volume 17, pages 994-999); further in view of Easterling et al. (Routine Parts-per-Million Mass Accuracy for High-Mass Ions: Space-Charge Effects in MALDI FTICR, Analytical Chemistry, 1 February 1999, Volume 71, Number 3, pages 624-632).

Yates and Gygi et al. are deficient in applying the method of identifying polypeptides from complex mixtures by mass spectrometry using genomic databases and quantitation of said polypeptides identified to an explicitly stated range of mass accuracies.

Easterling et al. examines the effect of ion space-charge on mass accuracy for mass spectra with broad distributions of mass ions and that part per-million mass accuracy can be obtained for ions over a broad mass range (Abstract; page 626, column 1, lines 33-40). The authors state the number of proteolytic fragment masses needed to identify a protein from a search of a sequence database has an inverse relationship to the mass accuracy of the data (page 624, column 1, line 7-10). Easterling et al. performs a number of calculations of mass error measurements and specifically indicates various part per-million mass accuracies (i.e. 0.07, 2.3, 4.2, 8.5, 63, 110, 141, etc.) and applies varying mass accuracies (Abstract; page 627, column 1, lines 4-34; page 630, column 2, lines 32-43; Tables 1 and 2).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the inventions was made to perform a wide range of mass accuracy measurements (100 ppm or greater, 10 ppm or greater, etc), as taught by Easterling et al. with Yates; taken in view of Gygi et al. a method of identifying polypeptides from complex mixtures by mass spectrometry using genomic databases and quantitation of said polypeptides identified in a single automated operation. Motivation for combining the above references is provided for by Easterling et al. which indicates that the described methodology calibration improves mass accuracy measurements in mass spectrometry by correcting differences in the number of ions thereby allowing for any type of sample to be examined by accounting for the total number of ions in the sample.

OBJECTION TO DISCLOSURE

The disclosure remains objected to because of the following informalities:

The disclosure contains an embedded hyperlink on page 32, line 26. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. It is suggested that "www.ncbi.nlm.nih.gov/GenBank" be replaced with "World Wide Web address: ncbi.nlm.gov/Genbank". See M.P.E.P. § 608.01 and 608.01(p).

Appropriate Correction Is Requested.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Channing S. Mahatan whose telephone number is (703) 308-2380. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina M. Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Date: June 30, 2003

Examiner Initials: CSM

Marianne P. Allen

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